REMARKS

Claims 1-10, 13-20 and 23-32 are pending. Claims 23-25 are withdrawn.

Rejection Under 35 USC §112, Second Paragraph

Claims 5 and 10 have been rejected as indefinite. However, in a telephonic interview on or about May 10, 2010, the examiner acknowledged that the rejection was improper in view of the claim amendments filed December 17, 2009. The rejection is therefore moot.

Rejection Under 35 USC §103(a)

Claims 1-5, 7, 14-20, 26 and 32 have been rejected as obvious over Junien (EP 1424070). Junien does not disclose any exemplary formulations combining metformin and a fibrate; rather, the only examples of co-administration are by gavage. The Office asserts that it would have been obvious to formulate the two active ingredients in the claimed ratios. Applicants respectfully disagree.

The present invention relates to formulations that give rise to high patient compliance by reducing the number of unit forms of administration that need to be taken since it provides a single pharmaceutical composition having a high amount of metformin with a fibrate in a smaller quantities, with a suitable size for oral administration. See, e.g., page 5 of the specification.

Generally, it is difficult to combine a hydrophilic active ingredient, such as metformin, with a poorly soluble, hydrophobic ingredient, such as a fibrate. Fenofibrate formulations currently on the market require a high amount of intra- and extra-granular excipients to maintain a sufficiently high dissolution rate. See, e.g., US 6,074,670, col. 5, ll. 3-4 (fenofibrate compositions contain 5-50% fenofibrate, preferably 20-45% by weight). In addition, since metformin does not compress well, a formulation containing metformin requires certain excipients to overcome the compressibility issue. Thus, one would expect the combination of these two active ingredients to require a very high proportion of excipients.

The skilled person seeking to prepare a pharmaceutical composition containing metformin and a fibrate would have been led by the prior teachings in the art to use large amounts of excipients, e.g., amounts greater than 50% by weight of the total composition. The skilled person would in particular have expected that a granulation diluent or "substrate" be

required to maintain the high surface area of fenofibrate granules, thereby maintaining a high dissolution rate of the fenofibrate. However, the inventors have unexpectedly found that if metformin and a fibrate are used in amounts such that the combined amount of active substances in the composition is from about 70% to 95% by weight, and the metformin : fibrate weight ratio is between 500:90 and 850:35, then each active substance demonstrates bioavailability that is similar to when each is administered in a single formulation.

Without wishing to be bound by theory, it appears that metformin acts to some extent as a carrier in the sense that it allows the manufacture of tablets of low excipient content which in particular retain the required high dissolution rate of fenofibrate, as evidenced by the examples. Particles of fibrate adhere to metformin particles. See, e.g., page 8, lines 18-21 of the specification. The bioavailability data shown in the present application verify that the active substances retain their therapeutic activity in the compositions.

Junien neither discloses nor suggests using metformin as a carrier for the fibrate in the compositions which contain both of these active ingredients. Junien only mentions methods for preparing the association of metformin and a fibrate in a general manner, for example by using conventional excipients well known to one skilled in the art. The only actual examples of co-administration in mice of the metformin and fibrate was by gavage. See, e.g., paragraph [0062]. Thus, Junien does not disclose any working examples of metformin and a fibrate formulated together in a single dosage form. Given the absence of any guidance from Junien, one of ordinary skill in the art at the time of the invention would not have expected that these two active ingredients could be successfully formulated together with less than 50% excipients, let alone about 5% to about 30% excipients, as recited in the claims.

Dependent claims 6, 8-10, 13 and 27-31 have been rejected as obvious over Junien in view of Stamm (US 6,531,158). Stamm fails to overcome the deficiencies of Junien, described above. Thus, for at least the reasons provided with respect to independent claim 1, dependent claims 6, 8-10, 13 and 27-31 are not obvious.

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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